

The patients had all been on our Research Ward for some time and had been involved in considerable study prior to the introduction of BOL 148. Their ways of responding to personnel, to one another, their daily variations, and the finer nuances of their psychotic ways of life were well known. For instance, two patients had double orientation and consciousness; one of these was aware of her double "life" and in the lucid phase, which was one of friendly, ready cooperation, coherence and honesty, could report on the other phase as one reports a dream.

In the testing situation the previously existing attitudes were maintained, and the same types and intensity of contacts were continued. Since the patients had been on medication trials previously, though not immediately preceding the BOL 148, it was natural to continue asking relevant questions.

Aside from the comments by two patients while on the lower dosage that they felt more refreshed by sleep, and food tasted better, there was no evidence of any psychic alterations in any of our subjects. It is particularly noted that the patient with double consciousness described above was unable to note any change in either of her phases of consciousness. That this was not due to the choice of fixed, unresponsive patients, was indicated by the fact that one of these patients later responded very well in milieu and psychotherapy, while two others reacted some weeks later to 50 microgram doses of LSD, just as other psychotic subjects have done in our experience (14).

We have been exploring chemical theories of schizophrenogenesis for some years. We recognize that the present study is indecisive

for any of these theories. It is, however, a weight in the balance, not in favor of any simple, direct, causal relationship between serotonin metabolism and schizophrenia. Beyond this we do not feel justified in going.

SUMMARY

BOL 148 administered to chronic schizophrenics, 1 mg. t.i.d. to 6 subjects for 2 weeks, or 5 mg. q.i.d. for 3 days to 3 subjects, had no evident effect on their psychoses.

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ADRENOCHROME IN BLOOD PLASMA

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The striking psychotomimetic effect of microgram quantities of lysergic acid diethylamide and the similarity of the induced experience to some clinical manifestations of schizophrenia has stimulated interest in the mechanism of LSD-25 activity. Physiological properties recently discovered for LSD-

25 suggest at least 3 possible mechanisms of activity—(A) an interference centrally with serotonin as a neurohormone (1), (B) interference with parasympathetic activity by inhibiting choline esterases (2), and (C) some disturbances in adrenaline metabolism (3).

The last two mechanisms and especially the third appears to account most satisfactorily

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for the clinical and physiological changes. Thus LSD-25 produces increases in the secretion of adrenaline(4), an increase in cellular activity of the adrenal medulla(5) and an increase in the concentration in plasma of adrenaline oxidases(6, 7).

In our laboratory LSD-25 given to 5 normal subjects (100 micrograms by mouth) and three sober alcoholics (200 to 300 micrograms) markedly increased adrenochrome levels in plasma as shown in the following table.

TABLE SHOWING ADRENOCROME LEVELS (μ g/LITER) IN PLASMA AFTER ORAL ADMINISTRATION OF LSD-25

Time	0	2	4	6	24	48
Adrenochrome (micrograms/liter) ...	50	164	157	103	81	54

The height of the adrenochrome levels at 2 to 4 hours after administration of LSD-25 coincides well with the height in intensity of the clinical response. Perceptual distortions are maximal during this period. Adrenochrome levels are normal after 48 hours.

The threefold increase in adrenochrome levels from normal values(8) in plasma using an accurate biochemical assay(9) as

well as the evidence for the psychotomimetic effects of adrenochrome(10) and adrenolutin(11) strongly suggests that one of the basic mechanisms of LSD-25 activity is the production of adrenochrome which is one of the mediators of LSD-25 activity. Another is the increase in parasympathetic tone or acetylcholine activity(12) as in mechanism B. A comprehensive report will be submitted.

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